

a peripheral, cell-free, region which immunoisolates the core yet allows material secreted by the cells to diffuse out of the implants. Barry discloses a method of preventing adhesion in articular sites following surgery by injecting a solution of alginate and cations into the intra-articular space.

Rejections over Atala A

Claims 1, 3-8, 11, 14-19 and 21 are rejected under 35 U.S.C. 102(a) as being anticipated by Atala A. The Applicants present herewith a Declaration under 37 CFR §1.132 to overcome this reference. In addition, copies of both Atala A and Atala B are enclosed herewith. The declaration, executed by Dr. Atala, states that Atala A was not available to the public at the October, 1992, Annual Meeting of the American Academy of Pediatrics. Applicants submit that claims 1, 3-8, 11, 14-19 and 21 are allowable in view of Atala A.

Claims 2, 9, 12, 20, and 22, which depend from claims 1 and 11, are rejected under 35 U.S.C. 103 as being unpatentable over Atala A, Nevo, Vacanti A, and, if necessary, in further view of Vacanti B. Applicant respectfully submits that this rejection is obviated by the above-mentioned Declaration that renders claims 1 and 11 allowable.

Rejections over Schlameus

Claims 1, 2, 4-8, 11, 12, 14-18, 20 and 22 are rejected under 35 U.S.C. 102(e) as being anticipated by Schlameus. Applicants submit that Schlameus fails to disclose an implant which, upon hardening, forms a three-dimensional open-lattice structure which entraps water molecules to form a hydrogel with dissociated cells, as recited by claim 11, or a method of introducing cells into an animal in which a cell-polymeric composition is hardened to form such a structure, as recited by claim 1. Instead, Schlameus discloses implanting microcapsules which incorporate an alginate solution and cells. These microcapsules do not harden to form a three-dimensional matrix, as recited by the instant claims. Applicants further submit that, because of the significant substantive differences between Schlameus and the claimed invention, it is not necessary to present evidence of prior invention; Applicants explicitly reserve the right to present such evidence in the future. As a result, Applicants submit that claims 1, 2, 4-8, 11, 12, 14-18, 20 and 22 are allowable over Schlameus.

Claim 3 is rejected under 35 U.S.C. 103 as being unpatentable over Schlameus in view of Barry and Dionne, and, if necessary, in further view of Bhatnagar. Applicant submits that there is no motivation to combine Schlameus and Barry. Barry discloses the injection of an alginate solution to prevent the formation of adhesions, which comprise fibrinous tissue. Schlameus discloses a medium to deliver cells to a injured site for tissue repair. It is unclear that the combination of Schlameus and Barry would accomplish the aims of both, as suggested by the Examiner (Paper 17, pg 7, lines 11-16). That is, a cell-containing alginate solution injected into a tissue site will be unable to prevent intra-articular adhesions outside of the tissue, and such a solution injected between two tissues will be unable to effect tissue repair in either because the matrix synthesized by the cells cannot be transported to the tissue. Indeed, it can be argued that the tissue produced by the cells in an intra-articular site may contribute to adhesion. Applicants submit that one skilled in the art would not reasonably expect success from a combination of Schlameus and Barry. In addition, Schlameus teaches against a combination with Dionne because, if the microcapsules are omitted, the rate of release of the unencapsulated materials cannot be controlled. Such control is disclosed in column 4, lines 63 through 68, and column 5, lines 5 through 8. While Bhatnagar discloses forming a hydrogel *in situ* for tissue repair, he does not provide any motivation for giving up the advantages of encapsulation disclosed by Schlameus so that it may be combined with Dionne or Barry. Therefore, Applicants submit that claim 3 is not obvious in view of Schlameus, Barry, Dionne and Bhatnagar, either separately or in combination.

Claims 9, 19, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schlameus, Nevo, and Vacanti A and, if necessary, in further view of Vacanti B. Applicant submits that the use by Nevo of implanted gels that are not in the form of microcapsules cannot possibly render obvious the formation of a molded implant having a desired anatomical shape. The teachings of Nevo, that a cell-containing composition can be pressed into a tissue site (column 3, lines 56-61), cannot provide motivation to mold such a composition instead of encapsulating it before delivery to a tissue site. Furthermore, Vacanti B suggests molding implants into disks and fibrils not anatomical shapes, as required by claim 9. Vacanti A, while disclosing that matrices can be molded into an anatomical shape, does not provide any motivation to give up the advantages of encapsulation cut by Schlameus. Indeed, there is no

suggestion in either Vacanti A or Vacanti B to mold a cell-containing composition. Applicants submit that no such suggestion is provided by Nevo or Schlameus, either, and that the combination of Schlameus, Nevo, and Vacanti A and B would not result in the claimed invention. Thus, Applicants submit that claim 9 is not obvious in view of Schlameus, Nevo, Vacanti A, and Vacanti B. Claims 19 and 21 depend from claims 8 and 18, which Applicants suggest are patentable.

Rejections under 35 U.S.C. 112

Claims 21 and 22 are rejected under 35 U.S.C. 112. The Examiner states that these claims recite "The method of claim 18" improperly because claim 18 is drawn to a composition. Applicants submit that claim 18 recites an implant. Claims 21 and 22 have been appropriately amended, and Applicants submit that the rejection is overcome.

In light of the foregoing Amendment and Remarks, Applicant respectfully submits that the present case is in condition for allowance. A Notice to that effect is respectfully requested.

A check for \$36 for the fee under 37 CFR 1.16(c) for two new claims over twenty is submitted herewith. A Petition for Extension of Time under 37 CFR 1.136 and the appropriate fee are submitted herewith. Please charge any additional fees associated with this filing, or apply any credits, to our Deposit Account No. 03-1721.

Respectfully submitted,



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